PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

02 JUN 2005

Applicant's or agent's file reference 144 PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/50891	International filing date *(day/month/year)* 25.11.2003	Priority date *(day/month/year)* 03.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K45/00		
Applicant INNOGENETICS N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.06.2004	28.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Langer, A Telephone No. +49 89 2399-7809

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/50891

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-26 as originally filed

Claims, Numbers

1-15 received on 11.11.2004 with letter of 10.11.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents. If not indicated otherwise, the relevant passages are those cited in the International Search Report.

D1: US-A-5 866 167 (VAN BOSSUYT HANS) 2 February 1999 (1999-02-02)
D2: US-A-5 387 415 (FREIDENREICH JURGEN ET AL) 7 February 1995 (1995-02-07)
D3: DATABASE WPI Section Ch, Week 199550 Derwent Publications Ltd., London, GB; Class B04, AN 1995-390237 XP002274804 & JP 07 267876 A (SUNSTAR CHEM IND CO LTD) 17 October 1995 (1995-10-17)
D4: US-A-6 046 178 (SILVETTI SR ANTHONY N) 4 April 2000 (2000-04-04)
D5: WO 97/41899 A (DRAYE JEAN PIERRE ;DELAEY BERNARD (BE); INNOGENETICS NV (BE); SCHA) 13 November 1997 (1997-11-13)

Document D1: Non-viable total keratinocyte lysate for promoting wound healing.
Document D2: Dried cryopellets containing Aloe vera extract, useful e.g. for accelerating wound healing, softening skin or having antibiotic action, and optionally further containing at least one additional skeleton forming hydrophilic material comprising xanthan, maltodextrin, pectin etc..
Document D3: Composition used in the treatment of regeneration of periodontal tissues or treatment of wounds, comprising cell growth factor and a water-soluble polysaccharide such as xanthan gum.
Document D4: A medication and method for treating wounds by contacting the wound with a therapeutically effective amount of a starch hydrolysate composition including trace elements (like copper and zinc) to beneficiate the wound healing processes. A possible starch hydrolysate is maltodextrin.
Document D5: A medicament containing a biopolymer matrix into which a therapeutically effective amount of a drug is non-covalently incorporated, wherein one of the active factors is e.g. keratinocyte cell lysate, said biopolymer matrix comprising gelatin cross-linked with an oxidized polysaccharide such as an oxidized xanthan. Preferably said medicament is a wound dressing.

2. Novelty (Art. 33 (2) PCT)

The technical features of **claims 1-15** are not disclosed by the prior art cited and therefore appear novel in terms of Art. 33 (2) PCT.

3. Inventive Step (Art. 33 (2) PCT)

The problem of the present application is to improve stability of cell lysate, in particular to solve the problem of sedimentation and flocculation after cell lysis.
A combination of the technical teaching of D1 and D5 with D2 to D4 prompts the skilled person inevitably into the direction of the presently claimed subject-matter.
The fact that the cited prior art does not specifically indicate the antiflocculation effect of xanthan does not confer inventive skill to the claimed compositions and processes as long as its addition to the composition of document D1 would still be obvious.
Claims 1-15 are therefore not inventive in terms of Art. 33 (3) PCT.

4. Industrial Applicability (Art. 33 (4) PCT)

For the assessment of the present **claims 11-15** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims (amended claims, 10 November 2004)

1. A pharmaceutical composition comprising a non-viable cell lysate and at least one antiflocculant and/or antisedimentation agent(s), wherein the antiflocculant and/or antisedimentation agent is xanthan gum.
2. The pharmaceutical composition of claim 1, wherein the antiflocculant and /or antisedimentation agent is a combination of xanthan gum and maltodextrin.
3. The pharmaceutical composition of claim 1 or 2 further comprising a buffering agent.
4. The pharmaceutical composition of claims 1 to 3 in a dried form.
5. The pharmaceutical composition of claims 1 to 3 in a freeze-dried form.
6. The pharmaceutical composition of claims 1 to 5, wherein the cell lysate is a keratinocyte cell lysate.
7. The pharmaceutical composition of claims 1 to 6, wherein said composition further comprises a pharmaceutically acceptable carrier/excipient/vehicle.
8. The pharmaceutical composition of claims 1 to 7 for the purpose of promoting wound healing, wherein said composition comprises a non-viable cell lysate and a pharmaceutically acceptable vehicle.
9. The pharmaceutical composition of claims 7 or 8, wherein said pharmaceutically acceptable vehicle is a dry powder, a suspension or a solution.
10. The pharmaceutical composition of claims 7 or 8 wherein said pharmaceutically acceptable vehicle is a gel, cream, ointment or a biocompatible matrix.
11. A process for the production of a homogenized pharmaceutical composition comprising the steps of growing, lysing and drying the cells, which process is characterized in that, immediately after lysing, antiflocculant and/or antisedimentation agents are added to stabilize the cell lysate mixture, wherein the antiflocculant/antisedimentation agent is xanthan gum.
12. A process of claim 11 wherein drying the cells is by freeze-drying.
13. A process of claims 11 or 12, wherein cell the lysate is a keratinocyte cell lysate.
14. A process of claims 11 to 13 wherein the antiflocculant and/or antisendimentation agent is a combination of xanthan gum and maltodextrin.
15. Use of the composition of claim 1 to 10 for the treatment of burn wounds or skin ulcers.